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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,094	09/12/2003	Kirsty Jane Dodgson	875.092US1	7668

21186 7590 12/05/2005

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,094	DODGSON, KIRSTY JANE	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *2-7,10-14,20-22,24 and 26-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,9,15-19,23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on September 14, 2005 is acknowledged. The traversal is on the grounds that groups I, III, IV and VI are related and that there is no serious search burden in searching the additional groups. This is not found persuasive because the inventions are distinct and unrelated, each from the other because of the reasons previously provided. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The methods are distinct as claimed because they have different methods steps; different functions and the effects have different final outcomes. For instance, each group is drawn to using different sample populations and having different steps which result in different effects and final outcomes. For instance, the use of at least one *vanA* and *vanB* specific oligonucleotide primers to detect or determine the presence or amount of amplified nucleic acid, is not necessary to practice the other methods. Contrary to applicants statements, group VI is separate and distinct, from groups I, III, IV or VI since only group VI comprises the use of at least one *vanA* and *vanB* specific oligonucleotide primers. Furthermore, only group I detects *vanA* in a sample by detecting or determining the presence or amount of hybrid formation. This method is separate and distinct from any other method. Therefore, each method is divergent with respect to the amounts of reagents used and their associated steps. For these reasons the inventions are patentably distinct.

Applicants' argue that there would be no serious burden on the Examiner to search for the other groups. However, in the instant case these inventions are distinct. The methods are distinct as claimed because they are drawn to measuring or performing different activities. Furthermore the distinct steps and products require separate and distinct searches. The groups have a separate status in the art as shown by their different classification. As such, it would be burdensome to search the inventions of groups together. Furthermore, a search for the invention of the groups would not be coextensive because a search indicating the process of one is novel or unobvious would not extend to a holding that the process of the other is novel or unobvious. Because of the different classifications of each group based upon the distinct method steps, a serious burden is imposed on the examiner to perform a complete search of the defined areas in both the patent and non-patent literature. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden on the examination of this application.

Applicants' argument that the groups are not distinct and are related is not found persuasive because contrary to applicants arguments the inventions have been shown to be distinct in view of: the different methods that require different components; the production of different effects; and the different capabilities of those functions as compared to the other groups. Contrary to applicants' arguments, each group has been shown to form a separate subject for inventive effort with an explanation indicates recognition of separate inventive effort by inventors. Also each distinct group shows the need for a separate field of search. Thus applicants' arguments are not persuasive

since each group has been shown to be distinct. Therefore applicants' argument that the search is not burdensome is not persuasive. The requirement is still deemed proper and is therefore made FINAL.

Amendment Entry

2. The amendment filed September 14, 2005 has been entered. Claim 9 has been amended. Claims 2-7,10-14, 20-22, 24, 27-43 have been withdrawn from consideration. Claims 1, 8-9, 15-19, 23 and 25-26 are under consideration in this office action.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

4. Claims 15-18 and 25 are objected to because of the following informalities: The claims are drawn to non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 8-9, 15-19, 23 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method to detect *vanA* in a sample, comprising: a) contacting a sample suspected of comprising amplified *vanA* nucleic acid with at least one *vanA* -specific oligonucleotide probe under high stringency hybridization conditions effective to form a hybrid between the *vanA* -specific oligonucleotide probe and *vanA* nucleic acid in the sample, wherein the *vanA* -specific oligonucleotide probe comprises sequence which include sequences substantially corresponding to nucleotides 870 to 896 of the *vanA* gene, the complement thereof, or a portion thereof, sequences substantially corresponding to nucleotides 851 to 868 of the *vanA* gene, the complement thereof, or a portion thereof, or sequences substantially corresponding to nucleotides 898 to 917 of the *vanA* gene, the complement thereof, or a portion thereof; and b) detecting or determining the presence or amount of hybrid formation.

The instant specification and claims are encompassing currently unidentified portions thereof. Therefore, there is evidence that claimed nucleotides have not yet

been identified. Moreover, the instant specification fails to disclose the specific portions thereof. In view of the lack of evidence, it is apparent that Applicants were not in possession of all or many portions thereof that would hybridize at the time of filing the instant application. The specification does not place any structure, chemical or absolute functional limitations on the portions thereof per se. The recitation of a portion thereof does not convey a common structure or function. The scope of the claims includes numerous structural variants and the genus is highly variant because a significant number of structural differences between the genus members are permitted. The specification fails to provide guidance on the structure of the portions thereof. Structural features that could distinguish molecules in the genus from others in the class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed.

The skilled artisan cannot envision the detailed structure of the portions thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the

scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Thus, in the absence of the description of portions thereof, the claims fail to meet the written description requirements.

The written description in this case only sets forth specific nucleotide sequences, therefore the written description is not commensurate in scope with the claims drawn to portions thereof. Neither the specification nor the claims teach how to define portions thereof. Neither the claims nor the specification teach how to obtain such portions. There is no guidance as to what the portions are; or what portions can or cannot be used in the method of detection being claimed. The specification does not include structural examples of portions thereof. Thus, the resulting portions could result in a complex not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named nucleotide sequences, the skilled artisan cannot envision the detailed structure of the portions thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere

statement that it is part of the invention and a reference to a potential method of isolating it. Therefore the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

6. Claims 1, 8-9, 15-19, 23 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The preamble of the claims is drawn to a method to detect *vanA* in a sample, however the recited steps within the method comprise a contact step and detecting or determining the presence or amount of hybrid formation. There is no correlation step which correlates detecting *vanA* in a sample to detecting or determining the presence or amount of hybrid formation. Therefore, the goal of the preamble is not commensurate with the steps of the method that are drawn to a method to detect *vanA* in a sample.

b) The claims refer to *vanA* -specific oligonucleotide probes comprising sequences which substantially correspond to nucleotides 870 to 896, nucleotides 851 to 868, and nucleotides 898 to 917 all of the *vanA* gene, however the claims fail to recite the reference sequence upon which the nucleotide fragments are based upon.

c) Furthermore, the nucleotide sequences should also refer to the corresponding sequence identification number (SEQ ID NO). Therefore clarification is required to overcome the rejection.

d) The phrase "high stringency" in the claim is a relative term which renders the claim indefinite. The phrase is not defined by the claim, the specification does not

provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. There are no requisite requirements regarding the reagent amounts, temperature, times and procedures with respect to the determination of high, medium or low stringency. Therefore the metes and bounds of the phrase cannot be ascertained. Thus, clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 8-9, 15-18, 23 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Petrich et al., (Mol. and Cellular Probes, 1999, Vol. 13:275-281). The claims are drawn to a method to detect *vanA* in a sample, comprising: a) contacting a sample suspected of comprising amplified *vanA* nucleic acid with at least one *vanA* -specific oligonucleotide probe under high stringency hybridization conditions effective to form a hybrid between the *vanA* -specific oligonucleotide probe and *vanA* nucleic acid in the sample, wherein the *vanA* -specific oligonucleotide probe comprises sequence which include sequences substantially corresponding to nucleotides 870 to 896 of the *vanA* gene, the complement thereof, or a portion thereof, sequences substantially corresponding to nucleotides 851 to 868 of the *vanA* gene, the complement thereof, or a

portion thereof, or sequences substantially corresponding to nucleotides 898 to 917 of the *vanA* gene, the complement thereof, or a portion thereof; and b) detecting or determining the presence or amount of hybrid formation. The dependant claims are drawn to physiological peri-rectal samples, probes which are not specific for *vanA*-specific probe and are *vanB* specific probe.

Petrich et al., teach direct detection of *vanA* and *vanB* genes in clinical specimens for rapid identification of Vancomycin Resistant Enterococci (VRE) using multiplex PCR. The assay combines an optimized procedure for specimen preparation, a sensitive multiplex PCR and a specific microtiter plate to detect *vanA* and *vanB* mediated resistance (page 276, col.1). Petrich et al., teach that the PCR amplification products are detected using a microtiter plate amplification detection assay and oligonucleotide probes for *vanA* amplification detection (page 277, col. 1). Specific oligonucleotides probes for *vanA*, named vanA3 is disclosed (page 277, col.1). The claims simply require a portion thereof of sequences substantially corresponding to nucleotides 851 to 868, 870-896, or 898 to 917 of the *vanA* gene, since the portion is not defined and Petrich et al., teach corresponding portions, it meets the limitations of the claims. The *vanA* and *vanB* probes were fluorescein-labelled using commercially available labeling and detection systems (page 277, col.2). Therefore the art teaches the use of *vanB* specific probes along with the use of labeled probes, just as claimed. The amplification product was denatured and allowed to anneal to the fluorescein-labelled oligonucleotide (page 277, col.2). The hybrid complexes were then captured onto a microtiter plate for detection of the complex (page 277, col. 2). The clinical

specimens were stool samples and rectal swabs from patients wherein the stool samples were processed as peri-rectal swabs (page 276. col. 2). Thereby teaching a physiological peri-rectal samples, just as required by the claims. Table 1 shows the comparison for the detection of *vanA* and *vanB* within the specimens (page 279).

Thus, Petrich et al., teach a method to detect *vanA* in a sample just as required by the claims.

8. Claims 1, 8-9, 15-19, 23 and 25-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Modrusan (US Patent 6,274,316).

The claims are drawn to a method to detect *vanA* in a sample, comprising: a) contacting a sample suspected of comprising amplified *vanA* nucleic acid with at least one *vanA* -specific oligonucleotide probe under high stringency hybridization conditions effective to form a hybrid between the *vanA* -specific oligonucleotide probe and *vanA* nucleic acid in the sample, wherein the *vanA* -specific oligonucleotide probe comprises sequence which include sequences substantially corresponding to nucleotides 870 to 896 of the *vanA* gene, the complement thereof, or a portion thereof, sequences substantially corresponding to nucleotides 851 to 868 of the *vanA* gene, the complement thereof, or a portion thereof, or sequences substantially corresponding to nucleotides 898 to 917 of the *vanA* gene, the complement thereof, or a portion thereof; and b) detecting or determining the presence or amount of hybrid formation. The dependant claims are drawn to a physiological peri-rectal samples, probes which are not specific for *vanA*-specific probe and are *vanB* specific probe.

Modrusan (US Patent 6,274,316) teach methods for detecting vancomycin resistant enterococci by cycling probe reactions. Methods are provided for determining the presence of vancomycin antibiotic resistant genes of enterococci in a biological sample, comprising the steps of (a) treating cells contained within the biological sample; (b) reacting the target single nucleic acids with one or more nucleic acid probes which are complementary to one or more portions of the antibiotic vancomycin resistant gene, under conditions, which allow the target and probe to hybridize to each other and form target-probe complexes; and (c) determining and detecting the presence of a vancomycin antibiotic resistant gene (col. 2, lines 28-46). The nucleic acid probes are complementary to a vancomycin resistant gene selected from the group consisting of *vanA, vanB, vanB2, vanC1, vanC2, vanC3, vanD*, or variants thereof (col. 2, lines 51-55).). Specific oligonucleotides probes for *vanA* and the other probes are disclosed within columns 12 and 13. The claims simply require a portion thereof of sequences substantially corresponding to nucleotides 851 to 868, 870-896, or 898 to 917 of the *vanA* gene, since the portion is not defined and Modrusan teaches corresponding portions, it meets the limitations of the claims. More than one probe may be utilized in order to multiplex, or detect more than one gene per reaction (col.2, lines 55-58). Representative examples of biological samples include clinical samples such as stool and peri-rectal abscess samples, which meets the limitations of the claims (col.5, lines 45-48). The probes may have one or more detectable markers attached to one or both ends (col. 6, lines 59-61). Modrusan teaches the design and synthesis of a probe for simultaneous detection of either the enterococcal *vanA* or *vanB* genes (col. 8-9, lines

45-32). Table 4 shows the use of *vanA* and *vanB* probes for the detection of targets, thus the art teaches comparing the presence or amount of hybrid formation of *vanA* to non-*vanA* hybrid complexes (col. 19, lines 55-26).

Thus, Modrusan teach a method to detect *vanA* in a sample just as required by the claims.

Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Palladino et al., (J.Clin. Micro, 2003) teach rapid detection of *vanA* genes directly from clinical specimens and enrichment broths by real-time multiplex PCR assay. Patel et al., teach multiplex PCR detection of *vanA, vanB, vanC-1,* and *vanC-2/3* genes in *Enterococci.* Petrich et al., (Diagnos. Micro. Infect. Disease) teach a multiplex PCR for detection of *vanA* from peri-rectal specimens. Roger et al., (J. Clin. Micro, 1999) teach a *vanA* specific PCR assay for the detection of vancomycin-resistant *Enterococcus faecium* from rectal and fecal samples. Satake et al., teach detection of vancomycin-resistance *Enterococci* in fecal samples by PCR.

Conclusion

10. No claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines

November 22, 2005

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